

12/3,K,AB/15 (Item 2 from file: 34)  
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Title: Hepatocellular **carcinoma** associated with adult-type  
citrullinemia  
Author(s): Ito T; Shiraki K (REPRINT) ; Sekoguchi K; Yamanaka T; Sugimoto K  
; Takase K; Tameda Y; Nakano T  
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Journal: DIGESTIVE DISEASES AND SCIENCES, 2000, V45, N11 (NOV), P  
2203-2206  
ISSN: 0163-2116 Publication date: 20001100  
Publisher: KLUWER ACADEMIC/PLENUM PUBL, 233 SPRING ST, NEW YORK, NY 10013  
USA  
Language: English Document Type: ARTICLE

Title: Hepatocellular **carcinoma** associated with adult-type  
citrullinemia  
, 2000  
...Identifiers--**ARGININOSUCCINATE SYNTHETASE**;

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DIALOG(R)File 55:Biosis Previews(R)  
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Growth inhibition of **melanoma** cell lines by an arginine depleting  
enzyme and its reversal by **argininosuccinate synthetase** gene  
overexpression

AUTHOR: Sarkar S; Arunakumari A; Wang M; Filpula D; Shorr R G L

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\*\*USA

JOURNAL: Proceedings of the American Association for Cancer Research Annual  
Meeting 37 (0): p418-419 1996 **1996**

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Cancer Research Washington, D.C., USA April 20-24, 1996; 19960420

ISSN: 0197-016X

DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster

RECORD TYPE: Citation

LANGUAGE: English

Growth inhibition of **melanoma** cell lines by an arginine depleting  
enzyme and its reversal by **argininosuccinate synthetase** gene  
overexpression

**1996**

...REGISTRY NUMBERS: **ARGININOSUCCINATE SYNTHETASE**;

DESCRIPTORS:

CHEMICALS & BIOCHEMICALS: ...**ARGININOSUCCINATE SYNTHETASE**;

05792422 PMID: 7061421

Regulation of glucocorticoids of arginase and **argininosuccinate synthetase** in cultured rat **hepatoma** cells.

Haggerty D F; Spector E B; Lynch M; Kern R; Frank L B; Cederbaum S D

Journal of biological chemistry (UNITED STATES) Mar 10 1982, 257

(5) p2246-53, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: AM-25983; AM; NIADDK; HD-06576; HD; NICHD; HD-11298; HD; NICHD

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We have examined and characterized the regulation by glucocorticoids of the levels of arginase and **argininosuccinate synthetase** in two rat **hepatoma** cell lines (H4-II-E-C3 and MH1C1). Hydrocortisone elevates the activity of both enzymes in a time- and dose-dependent fashion. This effect was blunted markedly by small amounts of ethanol (0.1 to 0.9% [v/v]) and blocked substantially by a high molar excess of the "anti-inducer" steroid fluoxymesterone. The other "optimal" inducers, dexamethasone and corticosterone were as effective as hy

253458 PMID: 6621518

Regulation of expression of genes for enzymes of the mammalian urea cycle in permanent cell-culture lines of hepatic and non-hepatic origin.

Haggerty D F; Spector E B; Lynch M; Kern R; Frank L B; Cederbaum S D

Molecular and cellular biochemistry (NETHERLANDS) 1983, 53-54

(1-2) p57-76, ISSN 0300-8177 Journal Code: 0364456

Contract/Grant No.: AM-25983; AM; NIADDK; HD-06576; HD; NICHD; HD-11298; HD; NICHD

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We present here the results of investigations conducted by ourselves and others on the regulation of the expression of genes encoding the enzymes of the mammalian urea cycle as manifest in cultured cells of both hepatic and extrahepatic origin. Upon consideration of the recently discovered discrete non-hepatic arginase genetic locus in man and our consequent hypothesis that the form of arginase thus transcribed in such extrahepatic cells functions principally in providing ornithine for protein anabolism and polyamine biosynthesis, rather than in detoxifying ammonia through urea formation, we have chosen instead to study permanent cell lines that are derived from liver and continue to perform a variety of hepatic functions in culture as experimental models for probing the molecular mechanisms underlying the control of ureagenesis within the mature liver cell. Of two such arginase-positive rat-**hepatoma** lines, we have characterized extensively in one (H4-II-E-C3) the mode of action of glucocorticoids in augmenting the cellular levels of this enzyme as well as of **argininosuccinate synthetase**. To this end, we have recently demonstrated that these stimulations are both mediated by binding of the hormones to classical cytoplasmic steroid receptors in a specific and saturable fashion and have thus concluded that the H4-II-E-C3 line will provide a suitable cell culture system for subsequent more detailed experiments from which the information garnered will continue to be relevant to the ureagenic pathway as modulated in the differentiated hepatocyte in vivo.

1983,

... the control of ureagenesis within the mature liver cell. Of two such arginase-positive rat-**hepatoma** lines, we have characterized extensively in one (H4-II-E-C3) the mode of action of glucocorticoids in augmenting the cellular levels of this enzyme as well as of **argininosuccinate synthetase**. To this end, we have recently demonstrated that these stimulations are both mediated by binding...

12/3,K,AB/8 (Item 8 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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05792422 PMID: 7061421

Regulation of glucocorticoids of arginase and **argininosuccinate synthetase** in cultured rat **hepatoma** cells.

Haggerty D F; Spector E B; Lynch M; Kern R; Frank L B; Cederbaum S D

Journal of biological chemistry (UNITED STATES) Mar 10 1982, 257

(5) p2246-53, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: AM-25983; AM; NIADDK; HD-06576; HD; NICHD; HD-11298; HD; NICHD

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We have examined and characterized the regulation by glucocorticoids of the levels of arginase and **argininosuccinate synthetase** in two rat **hepatoma** cell lines (H4-II-E-C3 and MH1C1). Hydrocortisone

elevates the activity of both enzymes in a time- and dose-dependent fashion. This effect was blunted markedly by small amounts of ethanol (0.1 to 0.9% [v/v]) and blocked substantially by a high molar excess of the "anti-inducer" steroid fluoxymesterone. The other "optimal" inducers dexamethasone and corticosterone were as effective as hydrocortisone in elevating the levels of these enzymes at saturating concentrations. Inhibition of these stimulations by cycloheximide indicated that ongoing cellular protein synthesis was required for both effects, and the admixture of extracts from fully stimulated and basal cells gave no evidence for the existence of direct inhibitors or activators of either enzyme. The results corroborate findings from earlier whole-animal studies and provide evidence for the following conclusions. (i) This stimulation by hydrocortisone of urea-cycle enzymes in the cultured **hepatoma** cells is mediated by a classical glucocorticoid mechanism involving initial binding to specific cytoplasmic steroid receptors and the eventual accumulation of new enzyme molecules. (ii) These cell lines thus constitute valid experimental models for use in further detailed studies on the molecular mechanism(s) through which glucocorticoids and intermediary metabolites effect a selective modulation of arginase and **argininosuccinate-synthetase** gene expression in the differentiated mammalian liver.

Regulation of glucocorticoid

12/3,K,AB/4 (Item 4 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)  
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08077983 PMID: 2538928

Paradoxical regulation of human **argininosuccinate synthetase** cDNA minigene in opposition to endogenous gene: evidence for intragenic control sequences.

Boyce F M; Pogulis R J; Freytag S O  
Department of Biological Chemistry, University of Michigan Medical School, Ann Arbor 48109-0606.

Somatic cell and molecular genetics (UNITED STATES) Mar 1989, 15

(2) p123-9, ISSN 0740-7750 Journal Code: 8403568

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Human somatic cell variants resistant to the arginine analog, canavanine, express 200-fold increased levels of **argininosuccinate synthetase** (AS) mRNA as compared to parental cells. In this study we examined whether AS cDNA sequences contain cis-acting regulatory elements that are involved in the induction of AS mRNA in canavanine-resistant cells. Minigene constructs containing AS cDNA sequences under the transcriptional control of a viral promoter were stably transfected into the human squamous cell **carcinoma** line, RPMI 2650. Upon conversion of cells to canavanine-resistance, expression of the endogenous AS gene increased by two orders of magnitude as expected. Surprisingly, however, expression of AS cDNA minigenes decreased 10- to 15-fold in canavanine-resistant cell variants. The observed down-modulation of AS cDNA minigene expression was dependent upon a concomitant induction of the endogenous AS gene and not simply expression of the canavanine-resistant phenotype. This paradoxical regulation was specific for AS gene sequences since a minigene containing the neomycin-resistance gene in place of AS cDNA sequences failed to regulate. Furthermore, minigenes lacking a substantial portion of the AS cDNA also failed to exhibit the down-modulation. These findings suggest that expression of the human AS gene is regulated by a specific and limiting, positively-acting, trans-acting mechanism in canavanine-resistant cells and that exogenous AS cDNA (mRNA) sequences can compete for this mechanism.

Paradoxical regulation of human **argininosuccinate synthetase** cDNA minigene in opposition to endogenous gene: evidence for intragenic control sequences.

Mar 1989,

... somatic cell variants resistant to the arginine analog, canavanine, express 200-fold increased levels of **argininosuccinate synthetase** (AS) mRNA as compared to parental cells. In this study we examined whether AS cDNA...

... the transcriptional control of a viral promoter were stably transfected into the human squamous cell **carcinoma** line, RPMI 2650. Upon conversion of cells to canavanine-resistance, expression of the endogenous AS...

12/3,K,AB/5 (Item 5 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)  
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07251229 PMID: 3020714

Expression of human **argininosuccinate synthetase** after retroviral-mediated gene transfer.

Wood P A; Partridge C A; O'Brien W E; Beaudet A L

Somatic cell and molecular genetics (UNITED STATES) Sep 1986, 12

(5) p493-500, ISSN 0740-7750 Journal Code: 8403568

Contract/Grant No.: GM27593; GM; NIGMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The cDNA sequence for human **argininosuccinate synthetase** (AS) was introduced into plasmid expression vectors with an SV40 promoter or Rous **sarcoma** virus promoter to construct pSV2-AS and pRSV-AS, respectively, and human enzyme was synthesized after gene transfer into Chinese hamster cells. The functional cDNA was inserted into the retroviral vectors pZIP-NeosV(X) and pZIP-NeosV(B). Ecotropic AS retrovirus was produced after calcium-phosphate-mediated gene transfer of these constructions into the packaging cell line psi-2, and viral titers up to 10(5) CFU/ml were obtained. Recombinant AS retrovirus was evaluated by detecting G-418-resistant colonies after infection of the rodent cells, XC, NRK, and 3T3. Colonies were also obtained when infected XC cells were selected in citrulline medium for expression of AS activity. Southern blot analysis of infected cells demonstrated that the recombinant retroviral genome was not altered grossly after infecting some rodent cells, while other cells showed evidence of rearrangement. A rapid assay for detecting AS retrovirus was developed based on the incorporation of [14C]citrulline into protein by intact 3T3 cells or XC cells.

Expression of human **argininosuccinate synthetase** after retroviral-mediated gene transfer.